PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

CABINET REGIMBEAU
20, rue de Chazelles
F-75847 Paris Cedex 17
FRANCE

NR

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	11.11.2004
Applicant's or agent's file reference 344918/20396	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB 03/03213	11.06.2003	11.06.2002

Applicant
ETHYPHARM et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Longo, E Tel. +49 89 2399-8141

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 344918/20396	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/03213	International filing date *(day/month/year)* 11.06.2003	Priority date *(day/month/year)* 11.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/51		
Applicant ETHYPHARM et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.01.2004	11.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Merkl, B Telephone No. +49 89 2399-2138

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/03213

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-51 as originally filed

Claims, Numbers

1-51 as originally filed

Drawings, Sheets

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-51
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-51
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-51
	No:	Claims	

2. Citations and explanations

   see separate sheet

Item V:

1. D1: WO 98/51284 A (IMARX PHARMACEUTICAL) 19 November 1998 (1998-11-19)
   D2: WO 99/30620 A (IMARX PHARMACEUTICALS) 24 June 1999 (1999-06-24)
   D3: WO 01/64328 A (MAINELAB) 7 September 2001 (2001-09-07)

2. D1 and D2 do not disclose nanocapsules. D3 differs in that the molar mass of the poly(ethyleneglycol) component used in the nanocapsules is smaller than 1000g/mol. Therefore the requirements of Art. 33(2) PCT (novelty) are regarded to be met.

3. The problem of the pending application was to provide a carrier for active principles which exhibits reduced toxicity compared to the free drug in solution, which exhibits stealth properties with respect to the immune system of the host and which is capable not only of undergoing extravasation into the tumor but also of releasing its content therein. D3 is regarded to represent the closest prior art as it also refers to nanocapsules for the treatment of cancer. The only difference is that in the pending application the amphiphilic derivative of polyethyleneglycol has a molar mass which is greater than or equal to 1000g/mol instead of 660g/mol. There was no hint in the prior art that the use of the polyethyleneglycol derivative having the higher molar mass would lead to a protection against opsonization and therefore improve stealth properties. Therefore the requirements of Art. 33(3) PCT (inventive step) are regarded to be met.

4. As the term nanocapsules has no well-defined meaning in the art concerning the the size of the capsule at the upper limit it is necessary to insert the definition of page 2, paragraph 2 of the size into claim 1 during the further prosecution of the application in the national/regional phases.